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Ways forward from a regulatory and NITAG perspective

SCIENTIFIC WORKSHOP ASSESSING POTENTIAL CONSEQUENCES OF MATERNAL IMMUNIZATION ON NEONATAL OUTCOMES

Zurich 7-8 June 2026

Dr. Marco Cavaleri
Head of Public Health Threats department, EMA

ICH
harmonisation for better health

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12 May 2025
EMA/CHMP/ICH/149462/2025
Committee for Human Medicinal Products

ICH E21 Guideline on inclusion of pregnant and breastfeeding individuals in clinical trials

Step 2b

Transmission to CHMP	12 May 2025
Adoption by CHMP	22 May 2025
Release for public consultation	04 June 2025
Deadline for comments	15 September 2025

HMA
Heads of Medicines Agencies

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2 February 2026
EMA/653036/2019

Guideline on good pharmacovigilance practices (GVP)

Product- or Population-Specific Considerations III: Pregnant and breastfeeding women and their children exposed in utero or via breastmilk

Draft finalised by the Agency in collaboration with Member States	27 November 2019
Draft agreed by the EU Network Pharmacovigilance Oversight Group (EU-POG)	29 November 2019
Draft adopted by Executive Director	4 December 2019
Release for public consultation	6 December 2019
End of consultation	28 February 2020
Revised draft agreed by the Agency's Pharmacovigilance Risk Assessment Committee (PRAC) and finalised by the Agency in collaboration with Member States	5 January 2026
Revised draft agreed by the Co-ordination Group for Mutual Recognition and Decentralised Procedures – human (CMDh)	26 January 2026

Passive surveillance – what is new

Drug Safety (2024) 47:1127–1136
https://doi.org/10.1007/s40264-024-01448-y

ORIGINAL RESEARCH ARTICLE

Identification of Pregnancy Adverse Drug Reactions in Pharmacovigilance Reporting Systems: A Novel Algorithm Developed in EudraVigilance

Cosimo Zaccaria[1] · Loris Piccolo[1] · María Gordillo-Marañón[2] · Gilles Touraille[1] · Corinne de Vries[1]

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Abstract

Introduction There is a need to strengthen the evidence base regarding medication use during pregnancy and to facilitate the early detection of safety signals. EudraVigilance (EV) serves as the primary system for managing and analysing information concerning suspected adverse drug reactions (ADRs) within the European Economic Area. Despite its various functionalities, the current format for electronic submissions of safety reports lacks a specific data element indicating medicine exposure during pregnancy.

Objective This paper aims to address the limitations of existing approaches by developing a rule-based algorithm in EV that more reliably identifies cases that are truly representative of an ADR during pregnancy.

Methods The study utilised the standardised MedDRA query (SMQ) 'Pregnancy and neonatal topics' (PNT) as a benchmark for comparison. Recognising that the SMQ PNT also retrieves healthy pregnancy outcomes, contraceptive failure, failed abortifacients as well as ADRs not associated with pregnancy, a novel algorithm was tailored to improve the accuracy of identifying suspected ADRs occurring during pregnancy.

Results Upon testing, the algorithm demonstrated superior performance, correctly predicting 90% of cases reporting an ADR during pregnancy, compared to 54% achieved by the SMQ PNT. The implementation of the algorithm in EV led to the retrieval of 202,426 cases.

Conclusion The development and successful testing of the novel algorithm represents a step forward in pregnancy-specific signal detection in EV. Because signals associated with pregnancy may be diluted in a large database such as EV, this study lays the groundwork for future research to evaluate the effectiveness of disproportionality methods on a more refined subset of pregnancy-related ADR reports.

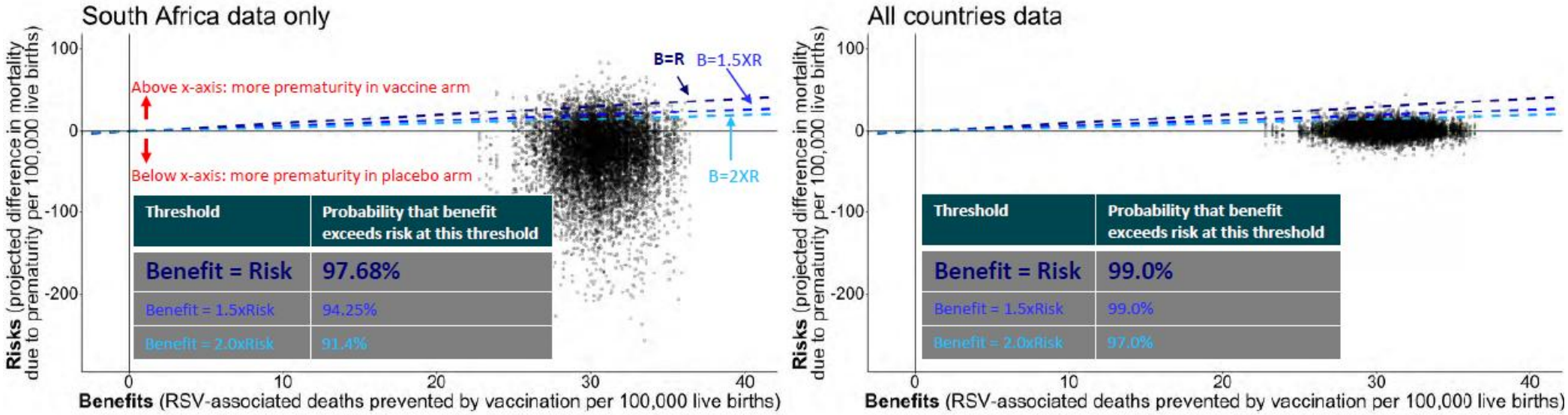
Benefit –risk modelling

Session3_RSV

Updated benefit-risk analysis with vaccination after 26 weeks GA

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Estimated risks and benefits of Abrysvo with trial birth outcomes born to mothers vaccinated at 27-36 weeks GA



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Benefit –risk balance

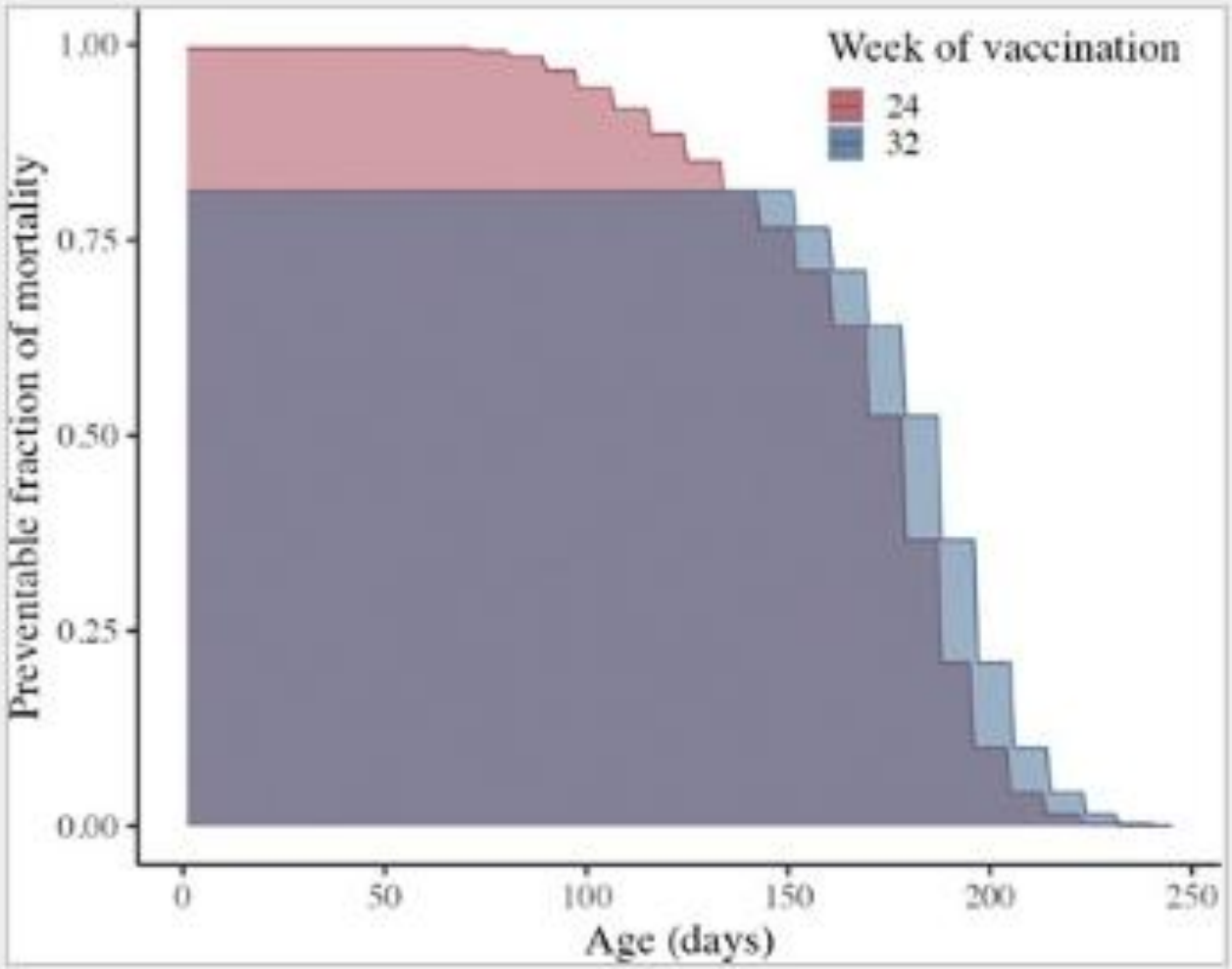

FIGURE 1.
The plot illustrates the maximal fraction of preventable RSV-related mortality cases across various infant age groups based on the RSV mortality data, assuming maternal vaccination occurs in either the 24th week (in red) or the 32nd week of pregnancy (in blue). In essence, it provides insight into the percentage of infants born with sufficient immunity to RSV acquired through maternal vaccination and tracks the gradual decline of this vaccine-induced immunity over time.

https://journals.lww.com/pidj/fulltext/2024/01000/disagreement_fda_and_ema_on_rsv_maternal.4.aspxtric Infectious Disease Journal

Example of labelling – VSV Ebola vaccine Ervebo

4.6 Fertility, pregnancy and lactation

Pregnancy

There are limited amount of data (less than 300 pregnancy outcomes) from the use of Ervebo in pregnant women, or women who became pregnant after receiving the vaccine. The safety of Ervebo has not been established in pregnant women.

As there are limitations to available data, including the small number of cases, caution should be exercised in drawing conclusions. Lack of reliable data on background rates of pregnancy and neonatal outcomes in the affected regions also makes a contextual assessment of the data challenging.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

As a precautionary measure, it is preferable to avoid the use of Ervebo during pregnancy. Nevertheless, considering the severity of EVD, vaccination should not be withheld when there is a clear risk of exposure to Ebola infection.

Pregnancy should be avoided for 2 months following vaccination. Women of child-bearing potential should use an effective contraceptive method.

EMA guidance for labelling for pregnancy and breastfeeding is focused on risk assessment

GUIDELINE ON RISK ASSESSMENT OF MEDICINAL PRODUCTS ON HUMAN REPRODUCTION AND LACTATION: FROM DATA TO LABELLING (2009)

- Guideline provides a risk-based approach:
- **"**information on the risks following exposure to the medicinal product before and during pregnancy, and during lactation should be provided as well as recommendations on the management of risk in clinical practice."
- Proposed template labelling language is based on size of safety database in pregnant women as well as outcome of non-clinical testing

	Non clinical data	
	Effects detected *	**No effects detected**
Human data	Conclusion from integration *Labelling* *(see appendix 3)*	Conclusion from integration *Labelling* *(see appendix 3)*
Demonstrated human teratogenicity (or fetotoxicity)	Proven risk in humans *Labelling [1]* *See also decision scheme on Contraindication*	Proven risk in humans *Labelling [1]* *See also decision scheme on Contraindication*
Supposed or suspected human teratogenicity (or fetotoxicity)	Strong suspicion of risk in humans *Labelling [2]*	Risk is possible in humans *Labelling [3]*
None or less than 300 prospective exposed pregnancies with known outcome in the 1st trimester and no increased rate of malformation identified	Risk is possible in humans, not confirmed *Labelling [4]*	Malformative risk unlikely in humans, but low evidence *Labelling [5]*
At least 300 prospective exposed pregnancies with known outcome in the 1st trimester and no increased rate of malformation identified	Malformative risk unlikely in humans, but low evidence *Labelling[6]*	Malformative risk unlikely in humans with moderate to substantial evidence *Labelling[7]*
At least 1000 prospective exposed pregnancies with known outcome in the 1st trimester and no increased rate of malformation identified	Malformative risk unlikely in humans with strong evidence *Labelling [8]*	Malformative risk unlikely in humans with strong evidence *Labelling [8]*

* Insufficient data are considered as effects detected

Revision of the guideline on risk assessment of medicinal products on human reproduction and lactation: from data to labelling

Concept paper on revision of the Guideline on Risk Assessment of Medicinal Products on Human Reproduction and Lactation: from Data to Labelling

- The Committee for Medicinal Products for Human Use (CHMP) and the Pharmacovigilance Risk 138 Assessment Committee (PRAC) has recommended the revision of the current Guideline.
- Update will include a revision of the terminology of standard statements for use in section 4.6 “Fertility, pregnancy and lactation” of the SmPC, with an aim to improve the information to health care professionals and patients. Furthermore, development of corresponding standard texts for the PL is planned for.

Way Forward

- Adjust current framework to include analyses beyond prematurity defined by the cut-off of 37 weeks GA in clinical trials to fully understand the clinical relevance and severity of any possible safety signal related to prematurity, e.g. time from vaccination to birth, very premature births

- Mechanistic explanation and biological plausibility of any safety signal whenever they occur are of major relevance to establish the strength of the safety signal

- Background rates of premature births should be determined in different part of the world using most rigorous and standardized evaluation of GA

- Standardised quality data collection, common protocols and analytic methods that allow data to be compared across systems are best forged through international partnerships, which can also catalyze academic work and may allow for global information sharing.

- Early joint interactions with international regulators is warranted to ensure alignment on clinical trial design

- Collaboration between regulators and NITAGs is also essential to ensure clinical trials capture outcome of interest for vaccine recommendations

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Thank you

Marco.cavaleri@ema.europa.eu

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